

Appl. No. : 09/627,647  
Filed : July 28, 2000

required by M.P.E.P. §608.01(q), Applicant has provided paragraph numbering in the substitute specification. Applicant has also included parentheticals indicating the number of times that each claim has been amended. The presence of two claims designated "Claim 57" has been corrected by renumbering the second Claim 57, filed in the Supplemental Amendment of October 10, 2001 as Claim 58 and the numbers and dependencies of the subsequent claims have been amended accordingly. The terminology "said biological sample" in Claim 11 and former Claim 64 (now renumbered as Claim 65) has been replaced with "a biological sample." In addition, former Claim 67 (now renumbered as Claim 68) has been amended to remove the terminology "several" and to recite that the claimed invention comprises more than one temperature regulated zone. Support for embodiments containing more than one termperature regulated zones can be found at page 27, lines 16-17. Accordingly, the above amendments (which are also included in the substitute specification) do not introduce new matter.

In view of the foregoing, Applicants respectfully submit that the application is in condition for allowance. If the Examiner has any questions regarding this matter, he is invited to telephone the undersigned so that the question is resolved.

The specific changes to the specification and the amended claims are shown on a separate set of pages attached hereto and entitled **VERSION WITH MARKINGS TO SHOW CHANGES MADE**, which follows the signature page of this Amendment. On this set of pages, the insertions are double underlined while the deletions are stricken through.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: Feb. 19, 2002

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Appl. No. : 09/627,647  
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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

1. (Amended) A device comprising:

a microfluidic substrate comprising at least one pathway for sample flow; and said microfluidic substrate further comprising at least one temperature regulated zone which is capable of cycling between at least two temperatures, said at least one temperature regulated zone being adapted to bring at least a portion of said sample pathway to said at least two temperatures while a sample is continuously flowing along said at least a portion of said sample pathway.

11. (Amended) The device of Claim 1, further comprising a detector for measuring a physicochemical property of said a biological sample.

12. (Amended) The device of Claim 1, wherein said at least one temperature regulated zone comprises a metal bar in fluid communication with a plurality of water sources containing water at said at least two temperatures, said metal bar being in thermal communication with said at least a portion of said sample pathway.

52. (New) The device of Claim 1, wherein said device comprises a microfluidic substrate comprising at least one temperature regulated zone which is capable of cycling between at least two temperatures, and at least one constant temperature zone.

53. (New) The device of Claim 1, wherein said device comprises a microfluidic substrate comprising several temperature regulated zones capable of cycling between at least two temperatures.

54. (New) The device of Claim 1, wherein said flowing sample goes through a plurality of temperature cycles as it travels through the temperature regulated zone.

55. (New) The device of Claim 8, wherein said channels are fed in series with different samples separated from each other by separators.

56. (New) The device of Claim 8 wherein the portion of the channel which crosses the temperature regulated zone is rectilinear.

57. (New) The device of Claim 1, wherein said device comprises one temperature regulated zone.

Appl. No. : 09/627,647  
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57.58. (Amended) The device of Claim 2, wherein the force generated by said force supplying member is pressure.

58.59. (Amended) The device of Claim 5758, further comprising a sample supplier which supplies a sample to said at least one pathway.

59.60. (Amended) The device of Claim 5859, further comprising at least one inlet basin positioned at a first end of said at least one pathway such that said sample supplier supplies said sample to said inlet basin and said sample travels from said inlet basin to said at least one pathway.

60.61. (Amended) The device of Claim 5960, further comprising at least one outlet basin positioned at a second end of said pathway.

61.62. (Amended) The device of Claim 6061, further comprising at least one reagent supplier positioned between said inlet basin and said outlet basin.

62.63. (Amended) The device of Claim 6162, wherein said device comprises a plurality of said pathways.

63.64. (Amended) The device of Claim 5758, wherein said microfluidic substrate consists essentially of silicon.

64.65. (Amended) The device of Claim 5758, further comprising a detector for measuring a physicochemical property of said a biological sample.

65.66. (Amended) The device of Claim 5758, wherein said thermal cycling zone comprises a metal bar in fluid communication with a plurality of water sources containing water at said at least two temperatures, said metal bar being in thermal communication with said at least a portion of said sample pathway.

66.67. (Amended) The device of Claim 5758, wherein said device comprises a microfluidic substrate comprising at least one temperature regulated zone which is capable of cycling between at least two temperatures, and at least one constant temperature zone.

67.68. (Amended) The device of Claim 5758, wherein said device comprises a microfluidic substrate comprising more than one several temperature regulated zoneszone capable of cycling between at least two temperatures.

68.69. (Amended) The device of Claim 5758, wherein said flowing sample goes through a plurality of temperature cycles as it travels through the temperature regulated zone.

Appl. No. : 09/627,647  
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69.70. (Amended) The device of Claim 6263, wherein said pathways comprise channels arranged in parallel, and wherein said channels are fed in series with different samples separated from each other by separators.

70.71. (Amended) The device of Claim 6970 wherein the portion of the channel which crosses the temperature regulated zone is rectilinear.